Remarks

New claims 15-24 were added. Support for the claims is found at least at page 7, line 23 to page 8, line 12; page 13, line 2 to page 15, line 22; and page 15, line 24 to page 15, line 8.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-10 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection.

Analysis

The Examiner alleges that the specification, while disclosing biodegradable poly(ester anyhydrides) containing random ester bonds, does not envision biodegradable poly(ester anhydrides) containing random amide bonds. Without making any admissions and solely for the purposes of facilitating prosecution, claim 1 has been amended to delete the phrase "amide bonds".

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 4-7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Analysis

The Examiner alleges that claim 1 requires the presence of amide bonds in the polymer. Claim 1 has been amended to delete any reference to amide bonds. Therefore, the Examiner's rejection is moot. However, applicant directs the Examiner's attention to the fact that random amide bonds were in the alternative in claim 1; the polymer contained random ester or amide bonds, not both. Claims 4-7 depends from claim 1 and specify that the polymer has random ester bonds. Accordingly, claims 4-7 are definite.

Rejection Under 35 U.S.C. § 102/103

Claims 1 and 6-8 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,756,652 to Storey *et al.* ("Storey"). Claims 1 and 6-8 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,414,381 to Griffin *et al.* ("Griffin"). Claims 1-7 and 10 were rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under 35. U.S.C. § 103(a) as obvious over Teomim *et al.*, *J. Biomed. Mat. Res.*, Vol. 45, Issue 3, 258-267 (1999) ("Teomim") or Domb *et al.*, *Acta Polymerica,* Vol. 49, Issue 10-11, 526-533 (Dec. 14, 1998) ("Domb"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 US 947

(1987); *Scripps Clinic & Research Found v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in Scripps, 18 USPQ2d at 1010:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . *There must be no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in Scripps, Id.:

> [A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was

not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986).

Analysis

Claim 1 has been amended to specify that the polymer is aliphatic. Support for the amendment is found through the specification, for example, at least at page 9, lines 23-26.

Storey

Claims 1, 6-8, 15, and 16 are novel over Storey

Storey describes biodegradable poly(ester-anhydrides) (abstract). Storey discloses that the polyester segment components can contain a homopolymer, copolymer, or terpolymer of biocompatible hydroxy acids, for example, lactic acid, glycolic acid, ε-hydroxycaproic acid and γ-hydroxyvaleric acid (col. 3, lines 27-31). Alternatively, Storey discloses, the polyester segments can be formed by copolymerization of a polyhydric alcohol and a biocompatible polycarboxylic acid (col. 3, lines 31-33). Storey discloses that most typically, such copolymers are formed between dihydric alcohols, for example, propylene glycol, and biocompatible dicarboxylic acids (col. 3, lines 33-36).

Storey does not disclose or suggest biodegradable poly(ester anhydrides) having random ester bonds in the polymer backbone. As shown in Figures 1 and 6, the ester linkages occur at regular intervals in the polyester blocks, and thus are not randomly situated along the polymer backbone. The anhydride linkage is introduced into the polyesters by reacting two equivalents of the polyester with diphenylchlorophosphate (*see* Figures 1 and 6). In contrast, the claimed

materials are typically prepared by reacting a polyanhydride prepolymer with a polyfunctional organic molecule to form functionalized polyanhydride oligomers of various lengths. The functionalized oligomers are repolymerized to form a polyanhydride having ester bonds randomly located throughout the polymer backbones. Storey does not disclose or suggest biodegradable poly(ester anhydrides) containing monomers derived from sebacic or dodecanedioic acid and ricinoleic acid as required by the claims 15 and 16. Accordingly, claims 1, 6-8, 15 and 16, as amended, are novel over Storey.

Random ester bonds are not inherent in the polymers described in Storey

The Examiner alleges that since Storey does not exclude the ester bonds from being random, such randomness of the ester bonds would be inherent. Applicant respectfully disagrees. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). In relying upon the theory of inherency, the Examiner has provided no basis in fact and/or technical reasoning to reasonably support such a determination as required. The fact that Storey does not explicitly exclude random ester bonds is irrelevant as to whether such a feature is inherent.

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established

by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). As discussed above, the polymers described in Storey do not contain random ester bonds, particularly in view of the fact that the ester bonds are not formed during polymerization. Random ester bonds are not inherent in the polymers described in Storey. Accordingly, claims 1, 6-8, 15 and 16, as amended, are novel over Storey.

Claims 17-24 are novel over Storey

As discussed above, Storey does not disclose or suggest biodegradable poly(ester anhydrides) having random ester bonds in the polymer backbone. Storey does not disclose or suggest biodegradable poly(ester anhydrides) having random ester bonds in the polymer backbone, wherein the copolymer contains monomers derived from ricinoleic acid and sebacic acid as required by independent claim 17 and the claims dependent thereon or the ratio of monomers derived from ricinoleic acid to monomers derived from sebacic acid as required by claim 18. Accordingly, claims 17-24, as amended, are novel over Storey.

Griffin

Claims 1, 6-8, 15, and 16 are novel over Griffin

Griffin describes a melt processable aromatic poly(ester-anhydride) (abstract). In contrast, the claimed biodegradable poly(ester anhydrides) are aliphatic. Griffin does not disclose each and every element of the claims. Accordingly, claims 1, 6-8, 15, and 16, as amended, are novel over Griffin.

Claims 17-24 are novel over Griffin

As discussed above, Griffin does not disclose or suggest biodegradable, aliphatic poly(ester anhyhdrides). Griffin does not disclose or suggest biodegradable, aliphatic poly(ester anhyhdrides) copolymer containing monomers derived from ricinoleic acid and sebacic acid as required by independent claim 17 or the ratio of monomers derived from ricinoleic acid to monomers derived from sebacic acid as required by claim 18. Claims 19-23 depend from claim 17. Accordingly, claims 17-24, as amended, are novel over Griffin.

Teomim

Claims 1-7, 10, 15, and 16 are novel over Teomim

Teomim describes polyanhydrides synthesized from ricinoleic acid half-esters with maleic and succinic anhydrides (abstract). The polymers described in Teomim are polyanhydride copolymers that are formed from the melt condensation of diacids and contain only anhydride bonds. Teomim does not disclose or suggest poly(ester-anhydrides) , let alone poly(ester-anhydrides) copolymers containing random ester bonds as required by independent claim 1 and the claims dependent thereon. Accordingly, claims 1-7, 10, 15, and 16, as amended, are novel over Teomim.

Claims 1-7, 10, 15, and 16 are not obvious over Teomim

Further, one of ordinary skill in the art would not be motivated to modify the polyanhydrides of Teomim to arrive at the claimed compositions. The claimed compositions contain a poly(ester-anhydride) containing random ester bonds in the polymer backbone. The

polymers are typically liquids at room temperature (page 7, lines 27-30) and thus can be administered by injection. The polymers release incorporated active agents over several weeks, which is longer than solid polymers prepared from the same monomers (page 7, lines 27-30). The slower release is due to the fact that when the polymer are placed in an aqueous medium (e.g., buffer solution, or tissue or biological mediums), the viscosity of the polymer increases (page 7, line 30 to page 8, line 3). This increase in viscosity results in a semisolid compact implant that keeps it integrity while slowly degrading and releasing incorporated drug (page 8, lines 3-6). These polymers also exhibited improved solubility compared to polyanhydrides (page 31, line 17 to page 32, line 2). The slower release of incorporated active agents and improved stability could not have been predicted from the polyanhydrides described in Teomim. Therefore, one ordinary skill in the art would not have been motivated to modify the polyanhydrides of Teomim to arrive at the claimed compositions. Accordingly, claims 1-7, 10, 15, and 16, as amended, are not obvious over Teomim.

Claims 17-24 are novel and non-obvious over Teomim

As discussed above, Teomim does not disclose or suggest poly(ester anhydrides) containing random ester bonds in the polymer backbone. Teomim does not disclose or suggest poly(ester anhydrides) containing random ester bonds in the polymer backbone containing monomers derived from ricinoleic acid and sebacic acid as required by independent claim 17 and the claims dependent thereon or the ratio of monomers derived from ricinoleic acid to monomers derived from sebacic acid as required by claim 18. Further, the properties of the polymers in the

claimed compositions could not have been predicted by Teomim. Therefore, one of ordinary skill in the art would not be motivated to modify Teomim to arrive at the claimed compositions. Accordingly, claims 17-23 are novel and non-obvious over Teomim.

Domb

Claims 1-7, 10, 15, and 16, as amended, are novel over Domb

Domb describes biopolymers for use as drug carriers and bioactive macromolecules (abstract). Domb discloses that polyanhydrides synthesized from non-linear hydrophobic fatty acid esters, based on ricinoleic acid, maleic acid, and sebacic acid allegedly possess desired physicochemical properties (page 526, 2nd column, 4th paragraph, lines 8-11). These polymers are polyanhydrides (i.e., contain only anhydride bonds), not poly(ester-anhydrides).

Domb also describes block copolyester-anhydrides (page 530, 1st col., 2nd paragraph). Domb describes ABA-type block copolymers of poly(propylene fumarate) (PPF) and lactide (page 530, 1st col., 3rd paragraph). The ester bonds in the block copolyester-polyanhydride polymers described in Domb are between the ester monomers units in the ester block (*see* structure 4 on page 530). These ester bonds are not random. In contrast, the polymers in the claimed compositions contain random ester bonds along the polymer backbone. Domb does not disclose each and every element of the claims. Accordingly, claims 1-7, 10, 15, and 16, as amended, are novel over Domb.

Claims 1-7, 10, 15, and 16 are not obvious over Domb

Further, one of ordinary skill in the art would not be motivated to modify the block copolyester-polyanhydrides of Domb to arrive at the claimed composition. The Examiner admits that Domb is silent regarding random ester bonds. However, the Examiner alleges that since Domb prepares the polymers with the same reactants in the same manner as the applicants, the random ester bonds are inherent. Applicants respectfully disagree. As discussed above, the copolyester-polyanhydrides described in Domb are block copolymers, wherein the ester bonds are between the monomer units in the ester block, not between anhydride blocks as in the claimed compositions. The ABA block copolymers described in Domb are prepared by ring opening polymerization of lactide using stannous octoate and PPF-diol as initiator (page 530, 1st col., 3rd paragraph). In contrast, the claimed compositions are prepared by reacting polyanhydride prepolymers with a polyfunctional organic molecule to form end-functionalized polyanhydride oligomers and then repolymerizing the oligomers to form poly(ester anhydrides) containing random ester bonds along the polymer backbone. The ABA block copolymers described in Domb are structurally different from the copolymers in the claimed composition.

Alternatively, the Examiner alleges that the randomness of the ester bonds within the polymer would be obvious because the preparation method of Domb does not exclude random ester bonds. Applicants respectfully disagree. As discussed above, the method of synthesis in Domb clearly excludes random ester bonds. Accordingly, claims 1-7, 10, 15, and 16, as amended, are not obvious over Domb.

The properties of the polymers in the claimed compositions could not have been predicted from Domb

As discussed above, the polymers in the claimed compositions are liquids at room temperature and release incorporated active agents over several weeks, which is longer than solid polymers prepared from the same monomers (page 7, lines 27-30). The slower release is due to the fact that when the polymer are placed in an aqueous medium (e.g., buffer solution, or tissue or biological mediums), the viscosity of the polymer (page 7, line 30 to page 8, line 3). This increase in viscosity results in a semisolid compact implant that keeps it integrity while slowly degrading and releasing incorporated drug (page 8, lines 3-6). The polymers also exhibit improved stability compared to polyanhydrides (page 31, line 17 to page 32, line 2). In contrast, the block copolyester-polyanhydrides described in Domb are described as being rubber-like, making them difficult to administer by injection. The ABA block copolyesters and the anhydride polymers described in Domb were degraded *in vitro* within four weeks. In contrast, the polymers in the claimed composition release incorporated active agents over a period of several weeks. The slower degradation times of the polymers in the claimed compositions could not have been predicted from the polyanhydrides and block copolyester-polyanhydrides described in Domb. Accordingly, claims 1-7, 10, 15, and 16, as amended, are not obvious over Domb.

Claims 17-24 are novel and non-obvious over Domb

As discussed above, Domb does not disclose or suggest poly(ester anhydrides) containing random ester bonds in the polymer backbone. Domb does not disclose or suggest poly(ester anhydrides) containing random ester bonds in the polymer backbone containing monomers derived from ricinoleic acid and sebacic acid as required by independent claim 17 and the claims dependent thereon or the ratio of monomers derived from ricinoleic acid to monomers derived from sebacic acid as required by claim 18. Further, the properties of the polymers in the claimed compositions could not have been predicted by Domb. Therefore, one of ordinary skill in the art would not be motivated to modify Domb to arrive at the claimed compositions. Accordingly, claims 17-23, as amended, are novel and non-obvious over Domb.

Rejection Under 35 U.S.C. § 103

Claims 1, 2, 3, 9, and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Storey, in view of U.S. Patent No. 5,648,096 to Gander *et al.* ("Gander") or U.S. Patent No. 5,626,862 to Brem *et al.* ("Brem"). Applicants respectfully traverse this rejection.

Legal Standard

"The proper analysis under § 103, was recently reviewed by the U.S. Supreme Court in KSR International, Inc. v. Teleflex, Inc, 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289. In KSR, the Court stated:

"If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, §103 likely bars its patentability. Moreover, if a technique

> has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions. Following these principles may be difficult if the claimed subject matter involves more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to the interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences, and creative steps a person of ordinary skill in the art would employ."

The Federal Circuit's decisions since KSR reflect an appropriately nuanced application of TSM analysis required by KSR and Graham. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1260 (Fed. Cir. 2007) (commenting generally on the implications of KSR for the Federal Circuit's obviousness assessments). Thus, where the claimed invention makes a routine addition of modern electronics to older devices, the Federal Circuit has found the requisite motive to

make the combination in the knowledge and ordinary creativity of a person of ordinary skill. See *In re Translogic Tech.*, 504 F.3d at 1262; *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1161 (Fed. Cir. 2007). Similarly, combinations of known options in the mechanical arts to solve the problem addressed by the claimed invention may make the invention obvious, for the person or ordinary skill would be motivated by the problem to try such combinations and achieve the same result. *In re Icon Health & Fitness, Inc.*, 496 F.3d 1374 (Fed. Cir. 2007).

In the chemical arts, where compounds are so similar as to create an expectation that the claimed new compound would have similar properties as the prior art compounds, the Federal Circuit also has upheld a finding that the claimed invention is not patentable. *Aventis Pharma Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1301 (Fed. Cir. 2007). However, when the prior art disclosed a broad selection of compounds that might have been potential candidates for further investigation, the lack of sufficient guidance and predictability to select the compound at issue supported a finding of nonobviousness. *Takeda Chem. Indus. Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1359-60 (Fed. Cir. 2007), petition for cert. filed, 76 U.S.L.W. 3374 (U.S. Dec. 20, 2007) (No. 07-838); see also *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007) (remanding to the Board, noting that despite close similarity of the claimed invention and prior art, rebuttal evidence to which the Board gave inadequate consideration showed unexpected results, a teaching away from appellant's invention and a long felt but unmet need).

Where there is structural similarity between a chemical compound and prior art compounds, the court notes that, "obviousness based on structural similarity thus can be proved

by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e., a lead compound) in a particular way to achieve the claimed compound." Slip Op. at 4 (citing *Takede Chem. Indus. v. Alpha Farm Pty., Ltd.*, supra, 492 F.3d at 1356). The Federal Circuit notes that, under KSR, what must be demonstrated is the possession of a sufficiently close relationship between the claimed and the prior art compound to create an expectation, in light of the entirety of the prior art, that the new compound will have similar properties to the old. (citing *Aventis Pharma Deutschland GmbH v. Lupin Ltd.*, supra, which relied upon *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc)). Thus, even though the prior art compound and the patented compound were virtually identical except for a substitution at a particular position on a pyridine ring, because expert testimony showed (1) there were significant differences between compounds that achieved anti-ulcer action and compounds that inhibited gastric acid and (2) the prior art compound provided a special path to achieve certain results, the prior art did not make the claimed compound obvious. There was no discernable reason for a skilled artisan to start with this "lead" prior art compound but then to modify it in a way that would eliminate an element of it to which this advantageous property was ascribed. Thus, it would not have been obvious to try certain substitutions in the chemical structure of the prior art compound to achieve the results found in the patented compound.

Even where the prior art suggests or motivates an inventor to develop the composition or process at issue, the Federal Circuit continues to recognize that there is a critical question under 35 U.S.C. § 103 as to whether the combined teachings of the prior art "would have given rise to a

reasonable expectation of success" in achieving what is claimed. *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007), petition for cert. filed, 76 U.S.L.W. 3393 (U.S. Jan. 2, 2008) (No. 07-888).

Storey in view of Gander or Brem

Storey is discussed above. Storey does not disclose or suggest a poly(ester-anhydride) containing random ester bonds along the polymer backbone as required by independent claim 1 and the claims dependent thereon. Domb does not disclose or suggest poly(ester anhydrides) containing random ester bonds in the polymer backbone containing monomers derived from ricinoleic acid and sebacic acid as required by independent claim 17 and the claims dependent thereon or the ratio of monomers derived from ricinoleic acid to monomers derived from sebacic acid as required by claim 18.

Gander and Brem disclose microimplants, such as microparticles, microspheres, and microcapsules can be used to encapsulate and deliver drugs. Gander and Brem, alone or in combination, do not cure the deficiencies of Storey. Accordingly, claims 1-10 and 15-24 are not obvious over Storey in view of Gander or Brem.

Allowance of claims 1-10 and 15-24, as amended, is respectfully solicited.

Respectfully submitted,

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